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# Safety of fluticasone propionate cream 0.05% for the treatment of severe and extensive atopic dermatitis in children as young as 3 months

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**Background:** Topical corticosteroids are useful for the treatment of pediatric dermatoses. However, concerns regarding possible systemic and topical toxicities have limited the use of moderate-potency corticosteroids in children.

**Objective:** Our purpose was to characterize the safety of fluticasone propionate cream in children.

**Methods:** Children between 3 months and 5 years 11 months ( $n = 32$ ) and 3 up to 6 years of age ( $n = 19$ ) with moderate to severe atopic dermatitis ( $\geq 35\%$  body surface area; mean body surface area treated, 64%) were treated with fluticasone propionate cream, 0.05% twice daily for 3 to 4 weeks. Serum cortisol response, fluticasone levels, skin changes, and adverse events were analyzed.

**Results:** Mean cortisol levels were similar at baseline ( $13.76 \pm 6.94$  g/dL prestimulation and  $30.53 \pm 7.23$  g/dL poststimulation) and at end of treatment ( $12.32 \pm 6.92$  g/dL prestimulation and  $28.84 \pm 7.16$  g/dL poststimulation). Only 2 of 43 children had end-treatment poststimulation values less than 18.0 g/dL. No significant adverse cutaneous effects were noted.

**Conclusion:** Fluticasone propionate cream 0.05% appears to be safe for the treatment of severe eczema for up to 4 weeks in children 3 months of age and older. (*J Am Acad Dermatol* 2002;46:387-93.)

Atopic dermatitis affects approximately 5% to 20% of all children by 11 years of age,<sup>1</sup> making it the most common skin disease of childhood.<sup>2</sup> Because of its chronic, recurrent nature, this form of eczema can have a considerable impact on the quality of life of patients and their families, including adverse effects on sleep patterns, behavior, family relationships, and financial stability.<sup>3</sup> Topical corticosteroids are commonly used to treat eczema.<sup>4</sup>

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## Abbreviations used:

ACTH:	corticotropin
ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
BSA:	body surface area
BUN:	blood urea nitrogen
CST:	cosyntropin stimulation test
FPIA:	fluorescence polarization immunoassay
HPA:	hypothalamic-pituitary-adrenal
HPLC:	high-pressure liquid chromatography
LDH:	lactate dehydrogenase
PUVA:	psoralen and ultraviolet light

Their misuse, however, may lead to skin thinning and systemic complications such as reversible hypothalamic-pituitary-adrenal (HPA) axis suppression. The occurrence of HPA axis suppression is of particular concern in children because of the potential for increased absorption caused by a higher ratio of skin surface area to body mass.

Topical formulations of fluticasone propionate (Cutivate, Glaxo Wellcome, Research Triangle Park, NC), a corticosteroid,<sup>5</sup> are indicated for the relief of

the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Both the cream and ointment formulations have shown minimal effects on HPA axis function in adults, as determined by measuring morning serum or plasma cortisol concentrations.<sup>6-9</sup> Any fluticasone propionate that is absorbed systemically is rapidly metabolized by the liver. The major metabolite of fluticasone propionate has no significant anti-inflammatory activity or glucocorticoid activity, contributing to its low potential for HPA axis suppression.<sup>10-12</sup> These unique pharmacologic characteristics suggest that fluticasone propionate may be appropriate for use in pediatric patients with extensive eczema in whom more potent corticosteroids are needed to suppress flares, but for whom HPA axis suppression is of concern.

Although the adrenal response to stimulation with cosyntropin (Cortrosyn; CST) has been tested in children after treatment with topical mometasone furoate,<sup>13</sup> no study in children has assessed the adrenal response to stimulation with cosyntropin after extensive treatment with topical fluticasone propionate. This information is important, given the recurrent nature of the disease and the need for safe, effective therapies for severe eczema in children. Thus the purpose of the present study was to evaluate the effects of fluticasone propionate cream 0.05% on HPA axis function using CST testing and to evaluate its effect on other safety variables in pediatric patients with moderate to severe eczema.

## MATERIALS AND METHODS

### Subjects

Pediatric patients between the ages of 3 months and 5 years 11 months with extensive moderate to severe psoriasis or eczema (excluding acute self-limiting eczema) were considered for enrollment. Their condition must have been stable or worsening and must have involved at least 35% of body surface area (BSA) (not counting lesions in the diaper area for subjects who wore diapers; also excluding lesions on the eyelids, in the perioral area, in the nostrils, and in areas where corticosteroid treatment was contraindicated). The total severity score was required to equal at least 6.0 for any 3 of 8 potential signs and symptoms (erythema, pruritus, papulation, induration, oozing/crusting, scaling, excoriation, lichenification), for which each sign/symptom was rated on a scale of 0.0 (absent) to 3.0 (severe).<sup>14</sup> BSA was estimated using the "rule of nines."<sup>15</sup> Subjects were stratified into 2 age groups: (1) 3 months to less than 3 years (younger group) and (2) 3 years to less than 6 years (older group). Written informed consent was obtained from the parent or guardian of all patients before study entry. Exclusion criteria included signifi-

cant disease other than the study disease; any gross physical impairment that would affect the outcome of or interfere with participation in the trial; any unstable concomitant disease other than the condition to be treated in the study; and known hypersensitivity to fluticasone propionate, its cream vehicle, or cosyntropin (Cortrosyn, Organon Inc, West Orange, NJ). Use or anticipated use of the following therapies also resulted in exclusion from the study: topical or inhaled corticosteroids within 1 week of study entry; long-term therapy (>4 weeks continuously) such as cyclosporine, methotrexate, psoralen and ultraviolet light (PUVA), or topical products for skin lesions within 4 weeks; systemic corticosteroids within 6 months; systemic retinoids; or any other topical or systemic therapy for the study disease other than bland emollients, such as moisturizers, in untreated areas, with the exception of therapies known to have no effect on cortisol values and HPA axis function. Patients who had engaged in certain recent activities (eg, the use of tanning booths, sunbathing, or UV light treatments) or who had potentially interfering personality characteristics or habits (subject or parent/guardian) during the study were also excluded. Participation in another investigational drug study within 4 weeks before the start of the study was not permitted.

### Study design

This phase IV open-label safety study was conducted at 10 centers in the United States. This study was approved by the Institutional Review Board at each center. Subjects were screened up to 6 days before baseline. After the baseline visit (day 1), visits occurred weekly for 3 to 4 weeks. At baseline and at the end of treatment visit, HPA axis function was determined by the response to CST, and blood was collected for clinical laboratory tests (serum chemistry, hematology, and assay of plasma fluticasone propionate concentrations). Proactive monitoring for adverse events, signs of skin atrophy, and skin pigmentation changes was conducted weekly. Subjects who had abnormal CST results, other laboratory abnormalities, or adverse events that required follow-up were seen 1 or 2 weeks after the end of treatment visit for repeat testing.

Fluticasone propionate cream 0.05% was applied twice daily to all lesions, including facial lesions, but not including those in the diaper area, eyelids, perioral area, nostrils, and areas in which corticosteroid treatment was contraindicated, such as those showing signs of atrophy. The amount necessary to cover the lesions was based on the fingertip unit, a ribbon of cream the length of the tip of the guardian's index finger (second phalanx).<sup>16</sup> The investigator was

expected to estimate the amount of cream that would make up the guardian's fingertip unit and to demonstrate to the guardian how much cream to apply based on the extent of BSA to be treated. Maximum drug exposure conditions were maintained by treating twice daily (fluticasone propionate 0.05% is currently approved for once- or twice-daily application in the treatment of atopic dermatitis) and continuing treatment for 1 week after subjects' lesional areas were assessed as cleared or for a maximum of 4 weeks. Clearing was defined as loss of signs or symptoms of disease and no residual erythema. A minimum of 35% BSA was treated regardless of healing for 3 to 4 weeks to maintain adequate conditions for testing the effects of systemic absorption of the drug and evaluation of local side effects. At each weekly visit, signs and symptoms of disease (eg, erythema, pruritus, papulation, induration, oozing/crusting, scaling, excoriation, and lichenification) were evaluated to monitor compliance and to assess the extent of exposure to study drug. Healed skin would be expected to absorb less study drug than diseased skin, although recently cleared lesional areas continue to exhibit less than normal barrier function.<sup>17</sup> In an effort to monitor compliance, all returned medication tubes were weighed.

### Safety assessments

Safety parameters included adrenal response to CST, signs of skin atrophy and pigmentation changes, changes in hematology and serum chemistries, and occurrence of adverse events. Plasma fluticasone values were measured only in subjects 2 years of age and older because of the limited amount of blood that could be drawn from younger subjects. A fasting blood sample was obtained for analysis of serum cortisol and clinical laboratory tests. Covance Central Laboratory Services, Inc, Princeton, New Jersey, performed all serum chemistries, hematology values, and cortisol measurements.

For the CST analyses, the baseline blood draw occurred on the morning of day 1, and the end-treatment blood draw occurred on day 22 or 29. Prestimulation blood samples were obtained at 8 AM. CST was administered intravenously immediately after prestimulation blood samples had been obtained. The dose of CST was 0.125 mg for subjects in the younger group and 0.25 mg for subjects in the older group. A poststimulation blood sample was obtained 30 minutes after the injection of CST. Subjects were offered food or drink after the administration of CST and before collection of the poststimulation sample. Serum cortisol was assayed by fluorescence-polarization immunoassay (FPIA) in all subjects and by high-pressure liquid chromatogra-

phy (HPLC) only in subjects 2 years of age and older, to minimize the amount of blood drawn from children younger than 2 years of age. For poststimulation CST results, the lower limit of normal for serum cortisol level was 18 g/dL for FPIA and 14.5 g/dL for HPLC. The minimal value detectable of cortisol was 1.0 g/dL for the FPIA method and 0.5 g/dL for the HPLC method.

The primary indicator of a normal adrenal response was defined as a poststimulation cortisol peak value of more than 18.0 g/dL by FPIA. The FPIA was chosen as the primary indicator of normal adrenal response because FPIA results were available to investigator sites within 24 hours of receipt. In addition, given the need to restrict HPLC analyses to the older age group because of blood volume concerns for the younger group, only FPIA values were available for all subjects. Of note is the correlation ( $>0.577$  and  $>0.85$  at 1 of 4 and 3 of 4 time points, respectively) between the cortisol data generated by the FPIA assay and HPLC assay ( $P < .001$ ) at each time point as determined by the Spearman correlation coefficient. Thus, had there been both FPIA and HPLC cortisol data for all subjects, data from either assay could have been used to evaluate adrenal function.

To assess consistency and to evaluate marginal responses, other criteria stated in the product information for CST were also examined, specifically, a prestimulation to poststimulation increase in cortisol of approximately 2-fold (provided the prestimulation value did not exceed the normal range) or an increase of 7 g/dL or more. CST results were also reviewed by a pediatric endocrinologist (D. B. A.).

Skin thinning and other signs associated with atrophy were assessed by 2 $\times$  magnification and included telangiectasia, loss of elasticity, purpura, dusky erythema, and striae. These signs were scored according to severity. Any pigmentation change not considered to represent a normal healing process was reported as an adverse event. Treated skin was assessed by the investigator at each visit. Baseline and end-of-treatment analyses of serum chemistries were performed for concentrations of alkaline phosphatase, lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose, total protein, albumin, sodium, potassium chloride, total carbon dioxide, phosphorus, uric acid, blood urea nitrogen (BUN), creatinine, calcium, and total bilirubin. Hematology assessment included white blood cell (WBC) count and differential, red blood cell (RBC) count and morphology, platelet count, hematocrit, and hemoglobin. Adverse events were recorded as to nature, severity, and relationship to study drug.

**Table I.** Summary of baseline demographic and subject characteristics

	Age 3 mo to 2 y	Age 3 to 5 y	Both age groups (total)
Age* (y)			
No.	32	19	51
Mean	1.7	4.4	2.7
SD	0.84	0.98	1.59
Median	1.7	4.2	2.5
Minimum	0.25	3.12	0.25
Maximum	2.99	5.86	5.86
Sex			
No.	32	19	51
Female	14 (44%)	10 (53%)	24 (47%)
Male	18 (56%)	9 (47%)	27 (53%)
Race			
No.	32	19	51
White	13 (41%)	7 (37%)	20 (39%)
Black	10 (31%)	5 (26%)	15 (29%)
Asian	5 (16%)	3 (16%)	8 (16%)
American Hispanic	1 (3%)	3 (16%)	4 (8%)
Other	3 (9%)	1 (5%)	4 (8%)
Height (cm)			
No.	28	18	46
Mean	81.4	103.5	90
SD	11.6	9.29	15.24
Median	84	102.5	90.5
Minimum	64	79	64
Maximum	101	122	122
Weight* (kg)			
No.	32	18	50
Mean	11.7	18.1	14
SD	2.86	3.23	4.28
Median	12	18.2	14
Minimum	7	12	7
Maximum	17	26	26

\*Age and weight were determined at the screening visit rather than at baseline.

Plasma fluticasone concentrations were determined by automated solid-phase extraction using a Zymark 96-well system (Zymark Corp, Hopkinton, Mass). The extracts were analyzed by HPLC with tandem mass spectrometric detection, using a reverse-phase column. The calibration range was 50 to 1520 pg/mL from 0.5 mL of plasma, with a limit of detection of 50 pg/mL.

### Statistical analysis

Data, including demographics, adverse events, and occurrence of atrophy and associated signs, were summarized using the intent-to-treat population consisting of the 51 enrolled subjects. The CST data presented are based on complete blood sample sets (baseline and end of treatment for prestimulation

**Table II.** Summary of baseline dermatologic characteristics\*

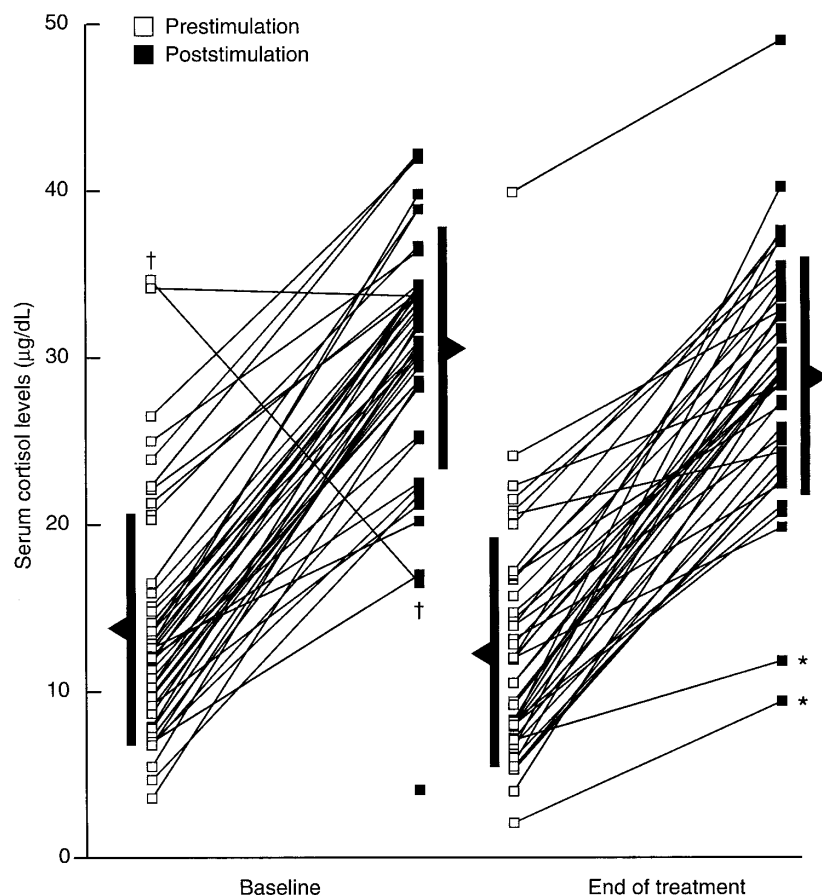
	Age 3 mo to 2 y	Age 3 to 5 y	Both age groups (total)
BSA covered by study disease (%)			
No.	32	19	51
Mean	65.3	71.1	67.7
SD	20.51	21.57	20.93
Median	66	76	71
Minimum	35	36	35
Maximum	100	100	100
BSA to be treated (%)			
No.	32	17	49
Mean	62.3	67.2	64
SD	17.81	20.15	18.59
Median	61	71	68
Minimum	35	36	35
Maximum	94	95	95
Sum of all signs/ symptoms			
No.	32	18	50
Mean	14.9	16.6	15.5
SD	3.88	4.68	4.21
Median	16	17	16
Minimum	9	8	8
Maximum	22	23	23
Cutaneous atrophy			
Blank	0 (0%)	1 (5%)	1 (2%)
No	32 (100%)	18 (95%)	50 (98%)
Yes	0 (0%)	0 (0%)	0 (0%)
Abnormal pigmentation			
Blank	0 (0%)	1 (5%)	1 (2%)
No	24 (75%)	15 (79%)	39 (76%)
Yes	8 (25%)	3 (16%)	11 (22%)

tion and poststimulation samples) available from 43 of the 51 subjects comprising the intent-to-treat population. CST results are presented for all subjects ( $n = 46$  prestimulation,  $n = 43$  poststimulation) with end-of-treatment CST (at day 22, day 29, or at the end of treatment for subjects who discontinued, regardless of treatment duration). Correlations using the Spearman correlation coefficient were also assessed between CST results and age, between the ratio of the amount of drug used to the BSA affected, and the ratio of the amount of drug used to the end-of-treatment poststimulation cortisol results.

## RESULTS

### Study population

Fifty-one children, 32 in the younger group (age 3-35 months; median, 20 months) and 19 in the older group (age 36-70 months; median, 50 months) were enrolled, all of whom had atopic dermatitis. In



**Fig 1.** Serum cortisol levels for all subjects at baseline ( $n = 49$  prestimulation,  $n = 47$  poststimulation) and end of treatment ( $n = 46$  prestimulation,  $n = 43$  poststimulation) with fluticasone propionate (for 22-30 days) before and after 30-minute CST stimulation as assessed by FPIA. Heavy black bars indicate mean  $\pm$  1 standard deviation. Asterisk, Children considered to have HPA suppression; dagger, apparent laboratory error.

the younger group, 8 children were younger than 12 months (4 were 3-6 months and 4 were 7-11 months). Demographic and baseline dermatologic characteristics are shown in Tables I and II, respectively. Subjects were evenly distributed between the sexes, and the majority were Caucasian (39%). The remaining children were African American (29%), Asian (16%), American Hispanic (8%), or other (8%). All children had a diagnosis of eczema at baseline, considered to be worsening in 76% of patients and stable in the remainder. The mean duration of the current eczematous episodes at this time was 45.7 weeks for the younger group and 107.7 weeks for the older group. The mean baseline BSA treated was 62.3%, with a range of 35% to 94% in the younger group and 67.2%, with a range of 36% to 95%, in the older group. The mean baseline BSA treated was 64% for all subjects. The average amount of drug used per day was 3.8 g (26.6 g/wk) in the younger

group and 7.7 g (53.9 g/wk) in the older group. At baseline, cutaneous atrophy was not reported for any child and only one child had telangiectasia (mild). Eight younger children (25%) and 3 older children (16%) had abnormal pigmentation.

Five children in the older group discontinued prematurely, 2 children before treatment because of inability to draw blood, and 3 children during treatment because of loss to follow-up (1 patient), inadequate disease severity at baseline (1), and an abnormal baseline CST (1). The 3 children who were discontinued during treatment were treated for less than 1 week.

#### Safety results

**Adrenal responsiveness.** The serum cortisol levels are presented in Fig 1. No meaningful differences were seen in mean prestimulation and poststimulation cortisol levels between baseline and the

end of treatment. Mean cortisol levels at baseline were 13.76 g/dL (standard deviation [SD], 6.94 g/dL) before stimulation and 30.53 g/dL (SD, 7.23 g/dL) after stimulation, and at the end of treatment these values were 12.32 g/dL (SD, 6.92 g/dL) before stimulation and 28.84 g/dL (SD, 7.16 g/dL) after stimulation (Fig 1). Furthermore, the mean differences between baseline and end of treatment in prestimulation and poststimulation cortisol values were small ( $-1.78$  g/dL,  $P = .1734$ ;  $-2.49$  g/dL,  $P = .0719$ , respectively).

Of the 43 children with end-of-treatment poststimulation cortisol values, only 2 (4.7%) had values that did not exceed 18.0 g/dL. The baseline values of these 2 subjects were 22.1 g/dL (prestimulation), 33.9 g/dL (poststimulation) and 10.8 g/dL (prestimulation), 28.6 g/dL (poststimulation). The end-of-treatment values were 7.1 g/dL (prestimulation), 11.8 g/dL (poststimulation) and 2.1 g/dL (prestimulation), 9.4 g/dL (poststimulation), respectively. These 2 children, 1 from each age group, were considered to exhibit HPA axis suppression. One of these children (age 5 years, 101 cm, 18.1 kg) had normal CST at follow-up, 12 days after the last dose of study medication (2.1 g/dL, prestimulation and 19.8 g/dL, poststimulation). This child had 95% BSA affected and was treated for a duration of 4 weeks (561.0 g of medication used). The other child (age 2 years, 91 cm, 13.1 kg), who had 35% BSA affected and was treated for a duration of 5 weeks (176.5 g of medication used), was lost to follow-up. The 5-year-old used more medication than the others in this age group (mean, 209.1 g), and the 2-year-old used more than the mean amount used in his age group (96.7 g) but less than the maximum amount of 355.7 g. These 2 subjects are shown in Fig 1 as the 2 points (indicated with an asterisk) with the lowest end-of-treatment poststimulation values.

Two other children in the younger group had end-of-treatment poststimulation cortisol levels indicating adrenal suppression by HPLC but not by FPIA. However, since the FPIA level trended low in one subject and did not show an increase of 7 g/dL or more in the other subject, it was noted that this possibly suggested evolving adrenal suppression in these 2 children. Of note is that the protocol exclusion criteria were violated by the use of long-term corticosteroid treatment in one child within 4 weeks of the study. Both of these children had a normal CST at the 2-week follow-up visit.

Finally, one investigator reported mild adrenal suppression in a child in the younger group. Owing to a laboratory error, this younger child's cortisol level was assessed by both FPIA and HPLC. The HPLC value, 17.2 g/dL, was thought to suggest sup-

pression using 18 g/dL as the lower limit of normal. However, the HPLC value was actually higher than 14.5 g/dL, the lower limit of normal for the HPLC assay. In addition, the FPIA prestimulation and poststimulation cortisol levels were normal, 13.1 g/dL and 22.4 g/dL, respectively, and the follow-up FPIA and HPLC prestimulation and poststimulation cortisol levels were also normal, so this child ultimately was not considered suppressed.

Very little correlation existed between age and either FPIA- or HPLC-generated cortisol data ( $P > .1$  at all time points; correlation coefficient [ $r$ ] of age with baseline and end of treatment for FPIA data,  $-0.20$  and  $-0.17$ , respectively; correlation coefficient [ $r$ ] with baseline and end of treatment for HPLC data,  $-0.16$  and  $-0.19$ , respectively). There was some correlation between the ratio of the amount of drug used to BSA affected and end-of-treatment poststimulation cortisol results ( $r = -0.40$ ;  $P = .02$ ).

**Relationship of plasma fluticasone concentrations to cortisol levels.** No child had measurable fluticasone values at baseline. Six of 25 children (24%) who had plasma samples taken at end of treatment for measurement of fluticasone had measurable concentrations of the drug, 3 in each age group. The mean fluticasone plasma concentrations were 112.1 pg/mL (range, 59-155 pg/mL) in the younger group, 163.1 pg/mL (range, 109-264 pg/mL) in the older group, and 137.6 pg/mL (range, 59-264 pg/mL) overall.

There were insufficient data to analyze relationships between plasma fluticasone concentrations and cortisol levels. However, detectable plasma fluticasone concentrations were present in only 1 of the 2 children considered to have adrenal suppression (plasma fluticasone concentration, 116.5 pg/mL (0.01165 g/dL), end-of-treatment poststimulation cortisol value, 11.8 g/dL) and in only 1 of the 2 children in whom there was the suggestion of evolving adrenal suppression (plasma fluticasone concentration, 122.0 pg/mL, end-of-treatment poststimulation cortisol value, 19.8 g/dL). The child with the highest plasma fluticasone concentration (264 pg/mL) did not have adrenal suppression (end-of-treatment poststimulation cortisol value, 23.3 g/dL).

**Adverse events involving the skin.** Twenty-five children (50%) had 39 adverse events, most frequently fever and cold symptoms. Only 7 drug-related adverse events were reported in 5 children. One event occurred in 1 subject in the younger group and 6 events occurred in 4 subjects in the older group (1 event in 3 subjects and 3 events in 1 subject). These 7 events were local events and included 1 event each of burning and urticaria (both resolved without action the day they were reported),

1 event of erythematous rash (resolved with discontinuation of the practice of applying drug to moist skin after bathing), and 3 events of telangiectasia (2 facial and 1 nonfacial). The facial telangiectasia in both subjects may have been a preexisting condition unmasked with resolution of the eczema. Both cases of facial telangiectasia were resolved within 1 month after cessation of study drug. In addition, 1 subject with facial and nonfacial telangiectasia also had mild dusky erythema, which resolved within 1 month after study drug cessation. Whether or not the nonfacial telangiectasia resolved is unknown.

No child had pigmentation changes assessed as treatment related, and fewer patients had abnormal pigmentation during and after treatment (11%-14%) than at baseline (22%).

There were no deaths, serious adverse events, or discontinuations caused by adverse events. There were no drug-related, clinically significant shifts in serum chemistry results or hematology values.

## DISCUSSION

This phase IV open-label study demonstrated that fluticasone propionate cream 0.05% applied twice daily for 3 to 4 weeks over a large BSA (mean, 64%) has a low potential to suppress HPA axis function in children as young as 3 months of age who have moderate to severe eczema. Infrequently, HPA axis suppression can occur, and therefore periodic monitoring is appropriate in high-risk patients. Monitoring may be carried out by CST, morning plasma cortisol levels, and urine-free cortisol tests. If HPA axis suppression occurs, withdrawal of the drug, reduction of the frequency of application, or substitution of a less potent steroid should be considered. Recovery of HPA axis function is generally rapid after discontinuation of topical corticosteroids. Rarely, signs and symptoms of glucocorticoid insufficiency may occur, requiring supplemental systemic corticosteroids. In this study, effects on the HPA axis were rapidly reversible in susceptible patients. There was no apparent relationship between plasma concentration and the development of adrenal suppression. Indeed, as noted earlier, the child with the highest plasma fluticasone concentration did not have adrenal suppression.

In addition, the results of this study suggest that fluticasone propionate cream 0.05% has a low potential for atrophogenic effects, even after extensive treatment with large quantities of the drug.

Fluticasone propionate cream 0.05% has an excellent safety profile when used in the treatment of moderate to severe atopic dermatitis for up to 4 weeks in children 3 months of age and older.

Specifically, it has a low potential for HPA axis suppression and for induction of atrophogenic effects, even after extensive application (mean baseline BSA treated, 64%).

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